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Anemia management in patients with chronic kidney disease: Taiwan practice guidelines and outcome analysis

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In Taiwan, the strategy of management of anemia in patients with CKD was different from many other parts of the world. In 1996, the National Health Insurance Administration of Taiwan applied a more restrictive reimbursement criteria for erythropoiesis-stimulating agents (ESA) use in patients with CKD. ESA is to be initiated when non-dialysis CKD patients have a serum creatinine > 6 mg/dL and a hematocrit <28% to maintain a hematocrit level a 30-33%. The maximal dose of epoetin-α or β was 20,000 U per month. The target hemoglobin range and dose limitation for ESAs were the same for dialysis patients. Thus, long before randomized controlled trials showing an increased risk for cardiovascular events at nearly normal hemoglobin concentrations and higher ESA doses in CKD, nephrologists in Taiwan had avoided the use of disproportionately high dosages of ESAs to achieve a hemoglobin level of 10–11 g/dL. Moreover, intravenous iron supplementation was encouraged earlier in Taiwan in 1996, when we reached consensus on the diagnostic criteria for iron deficiency (serum ferritin <300 ng/mL and /or transferrin saturation <30%). The experience of CKD anemia management in Taiwan demonstrated that a reasonable hemoglobin target can be achieved by using the lowest possible ESA dose and intravenous iron supplementation.

Later, the influence of these policies has been validated in Taiwanese dialysis patients. We assessed the association of anemia and iron parameters with mortality among the prevalent hemodialysis patients (AIM-HD) and peritoneal dialysis patients (AIM-PD) in Taiwan. Based on the Taiwan Renal Registry Data System (TWRDS) from 2001, to 2008, we found that a hemoglobin level lower than 10 g/dL was significantly associated with higher risk for all-cause and cardiovascular deaths. Moreover, serum ferritin level between 300-800 ng/mL and transferrin saturation (TSAT) value between 30-50% were associated with the lowest all-cause mortality in HD. Similarly, we also demonstrated that a hemoglobin level lower than 10 g/dL was significantly associated with a higher risk for all-cause and cardiovascular deaths. Moreover, a serum ferritin level higher than 800 ng/mL was associated with a higher risk for all-cause deaths, and a TSAT value between 20-50% was associated with the lowest all-cause mortality in PD.

Finally, a risk/benefit analysis of iron supplementation in pre-dialysis advanced CKD patients has not been conducted. Based on the Taiwan National Health Insurance Research Database from 2000 to 2009, we assess the effectiveness and the safety of iron supplementation in patients with CKD stage 5 who have not yet received dialysis (CKD 5 ND). We found that iron supplementation is associated with 15% risk reduction in death among CKD 5 ND patients who received ESA treatment. The survival benefit of iron use was consistent across the majority of dosage groups, except for those who were treated with monthly intravenous iron more than 200 mg. All above mentioned study outcomes in patients under dialysis and CKD5 ND will be added the revised Taiwan Chronic Kidney Disease clinical Guidelines 2021.